

**UNITED STATES DISTRICT COURT FOR THE
WESTERN DISTRICT OF NORTH CAROLINA
CHARLOTTE DIVISION**

VAIBHAVI PATEL,

Plaintiff,

vs.

GLAXOSMITHKLINE CONSUMER
HEALTHCARE HOLDINGS (US) LLC d/b/a
HALEON US, INC., PFIZER, INC. d/b/a
PFIZER CONSUMER HEALTHCARE, LLC,
WYETH, LLC, AND WYETH CONSUMER
HEALTHCARE, INC.,

Defendants.

Case No. _____

JURY TRIAL REQUESTED

PLAINTIFF'S ORIGINAL COMPLAINT

TABLE OF CONTENTS

I.	Parties	1
II.	Jurisdiction and Venue.....	1
III.	Facts	2
	A. Overview.....	2
	B. Relationship Between Defendants and Advil	4
	C. The Importance of SJS and TEN.....	5
	D. Laws Governing the Approval and Labeling of Pharmaceutical Drugs	6
	E. Defendants Have Known for Decades that Ibuprofen Causes SJS/TEN	8
	F. Newly Acquired Safety Information.....	9
	i. Undisclosed Cases of SJS and TEN (1985-2003).....	10
	ii. The French Query (2003).....	12
	iii. The Citizen’s Petition and Advil Label Change (2005)	13
	iv. Additional Scientific Literature Reporting an Increased Risk of SJS/TEN (2010-2022).....	16
	v. Female Subpopulation at Increased Risk of SJS/TEN	21
	vi. South Asian / Indian Subpopulation at Increased Risk of SJS/TEN	23
	vii. Defendants Failed to Fully Report and Disclose Adverse Events and Safety Signal Analysis to the FDA	24
	G. Conflict Between the Label and Medication Guide.....	27
IV.	Causes of Action	29
	A. Negligence	29
	B. Negligent Misrepresentation	30
	C. Gross Negligence.....	32
	D. Unfair and Deceptive Trade Practice-Misrepresentation.....	33

V.	Demand for Jury Trial.....	34
VI.	Request for Relief	34

Plaintiff Vaibhavi Patel (“Plaintiff”) files this Complaint against Defendants GlaxoSmithKline Consumer Healthcare Holdings (US) LLC d/b/a Haleon US, Inc. (“GSK”), Pfizer, Inc. d/b/a Pfizer Consumer Healthcare, LLC (“Pfizer”), and Wyeth LLC and Wyeth Consumer Healthcare LLC (collectively “Wyeth”).

I. PARTIES

1. Plaintiff Vaibhavi Patel is a citizen and resident of Matthews, North Carolina.
2. Defendant Glaxosmithkline Consumer Healthcare Holdings (US) LLC d/b/a Haleon, Inc. is a Delaware corporation with its principal place of business at 184 Liberty Corner Road, Suite 200, Warren, New Jersey 07059.
3. Defendant Pfizer is a Delaware corporation with its principal place of business at 235 East 42nd Street, New York, New York 10017.
4. Defendant Wyeth LLC, a subsidiary of Pfizer, is a Delaware limited liability company with its principal place of business at 5 Giralda Farms, Madison, New Jersey 07940.
5. Defendant Wyeth Consumer Healthcare LLC, a subsidiary of Pfizer, is a Delaware limited liability company with its principal place of business at 5 Giralda Farms, Madison, New Jersey 07940.

II. JURISDICTION AND VENUE

6. This Court has subject matter jurisdiction over this lawsuit pursuant to 28 U.S.C. §1332 because there is diversity of citizenship between the parties and the amount in controversy exceeds \$75,000, exclusive of interest and costs. The Court has jurisdiction over Defendants because they engaged in business in this judicial district in connection with the transactions and occurrences giving rise to this action, and because the wrongful conduct challenged herein was directed at, took place in, and/or had foreseeable injurious effects in this judicial district and the

State of North Carolina. The Court also has jurisdiction over Defendants because they have sufficient minimum contacts in North Carolina and intentionally avail themselves of the markets within North Carolina through the promotion, sale, marketing, and distribution of their products in North Carolina, thus rendering the exercise of jurisdiction by this Court proper and necessary. Each Defendant is licensed to conduct and systematically and continuously conducts business in North Carolina, including but not limited to marketing, advertising, selling, and distributing drugs to residents of North Carolina. Defendants have continuously and systematically engaged in business in this judicial district and the State of North Carolina such that they have subjected themselves to personal jurisdiction in this Court for all purposes.

7. Venue is proper in this judicial district pursuant to: (i) 28 U.S.C. §1391(b)(2) because a substantial part of the events or omissions giving rise to the claim occurred in this judicial district; and (ii) because Defendants regularly and systematically conduct business in this judicial district including, without limitation, the transactions at issue in this action. Venue is also proper in this judicial district pursuant to 28 U.S.C. §1391(a)(2) because Plaintiff's claims arose from events taking place within this judicial district and Plaintiff was injured and resides in this judicial district.

III. FACTS

A. Overview

8. Plaintiff was a healthy 26-year-old woman when she suffered a severe Stevens-Johnson syndrome ("SJS") and toxic epidermal necrolysis ("TEN") adverse drug reaction to Advil (ibuprofen). SJS and TEN are life-threatening and permanently disabling skin reactions with mortality rates ranging from 30% to as high as 80%.¹

¹ SJS is a serious adverse skin reaction in which skin in the affected areas dies and sloughs off in conjunction with a host of catastrophic symptoms. When more than 30% of the skin is involved, the SJS reaction is classified as TEN.

9. On October 31, 2021, following approximately two weeks of Advil use in October,² Plaintiff developed a skin rash that quickly progressed to SJS/TEN. Plaintiff's SJS/TEN reaction was catastrophic by any measure. It resulted in a multi-week hospitalization in the Wake Forest Burn Center; severe ocular complications in both of her deteriorating eyes; permanent scarring across her face and the majority of her body; post-traumatic stress disorder and depression; and pulmonary and gynecological injuries, among other permanent and disabling medical conditions.

10. There can be no legitimate dispute that Advil caused Plaintiff's SJS/TEN given:

- Plaintiff's medical records repeatedly identify Advil (ibuprofen) as an allergy and the cause of her SJS/TEN.
- Plaintiff's treating burn surgeon at Wake Forest, as well the Director of the Wake Forest Burn Center, have identified Advil as the cause of Plaintiff's SJS/TEN.
- A Lymphocyte Toxicity Assay ("LTA") laboratory test confirmed that Advil caused Plaintiff's SJS/TEN.³

11. Defendants have known for decades that Advil causes SJS and TEN. Throughout that time, they have taken consistent, calculated steps to downplay and conceal the known causal connection from regulators and consumers around the world. In the U.S., they have knowingly misled consumers and the FDA by withholding and selectively reporting key safety data since at least the early 1980s. Contrary to overwhelming scientific safety data, their own internal documents, and the opinions of their highest-ranking safety officers, Defendants have misrepresented (and continue to this day to misrepresent) to the FDA that the association between SJS and ibuprofen is "tenuous at best." They have made inconsistent decisions about whether and

² Plaintiff used Pfizer-labeled Advil Liqui-Gels as directed by Defendants and stopped using Advil at the first sign of her drug reaction.

³ An LTA test is a laboratory immunogenetic test that analyzes the patient's blood sample against a medication to determine toxicity (allergy). The LTA has repeatedly survived expert challenges in SJS/TEN cases.

to what extent to warn of the known risks of SJS/TEN from Advil on a country-by-country basis based on their analysis of the resulting civil liability exposure in a given country.

12. “There is an inherent tension between the desire for profit and scientific decisions that suggest warnings may well shrink the customer base because of the cautionary tone struck by the warnings.” *Hodges v. Pfizer, Inc.*, 14-cv-4855, 2015 WL 13804602, at *10 (D. Minn. Dec. 17, 2015) (another permanent injury Advil SJS/TEN case handled by Plaintiff’s counsel). That same profit motive drove Defendants’ conduct that caused Plaintiff’s injuries in this case. Advil is one of the most heavily-marketed and profitable drugs in Defendants’ history. As a result of their unprecedented direct-to-consumer advertising campaigns, Defendants have collectively reaped billions of dollars from Advil sales. Defendants’ aggressive Advil marketing campaign and the resulting sales also resulted in an increased number of adverse reactions to their drug, including a spike in cases of SJS and TEN.

B. Relationship Between Defendants and Advil

13. Wyeth brought Advil to market in 1984, almost 40 years ago. In 2009, Pfizer purchased Wyeth and its Advil products for \$68 billion. Since the 2009 acquisition, Wyeth has been a wholly owned subsidiary of Pfizer. From 2009 to 2019, Pfizer and Wyeth were jointly responsible for safety reporting and analysis for Pfizer’s consumer healthcare products, including Advil.

14. In August 2019, Pfizer and GSK created a joint venture, CH JVCo, owned 32% by Pfizer and 68% by GSK. From August 2019 through the time of Plaintiff’s injury in November 2021, Pfizer and GSK jointly controlled all Advil-related regulatory compliance, safety, labeling, sales and marketing functions, and shared the profits from Advil. During that time period, Pfizer continued to store all Advil adverse events in its safety database, maintained lead responsibility

for safety reporting to the FDA, and continued to manufacture and label Advil (including the Advil used by Plaintiff) as Pfizer products.

15. In July 2022, GSK and Pfizer created Haleon – a new company used to sell Pfizer and GSK’s consumer healthcare products. Pfizer and GSK continue to oversee and manage the manufacturing labeling and safety of Advil products through a series of internal agreements such as Safety Data Exchange Agreements, Transition Services Agreements, the Pfizer SAPA, the Pfizer Relationship Agreement, and through Pfizer and GSK’s positions on Haleon’s board of directors.

C. The importance of SJS and TEN

16. Due to the magnitude of injury and high mortality rates, SJS and TEN are two of the most serious and scrutinized adverse drug reactions. Stern, R.S., et al. 21 AM. J. ACAD. DERMATOL. 317-322 (1989) (commenting that because of high mortality/morbidity SJS/TEN is the most important drug-related cutaneous eruption with respect to assessing risk vs. benefits of drugs); Mockenhaupt et al., 128 J. INVEST. DERMATOL. 35-44 (2007) (“...SJS and TEN have a significant impact on public health because of high mortality, frequently lasting disability”); Roujeau et al., 333 N.E.J.M. 1600-1607 (1995) (“Although infrequent, these conditions [SJS and TEN] may kill or severely disable previously healthy people. A few cases have prompted the withdrawal of newly released drugs.”).

17. SJS/TEN’s impact on public health is unquestionably important. It has been reported that the costs associated with the treatment of SJS/TEN patients in the United States alone exceeds \$125 million per year – five times higher than the cost associated with any other hospital admission. Hsu, et al., “Morbidity and Mortality of Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis in United States Adults,” J. INVEST. DERMATOL. (2016).

18. It is therefore not surprising that the FDA requires drug companies such as Defendants to pay special attention to these potentially fatal serious adverse drug reactions (a clinically significant risk under FDA regulations) in order to reduce the number of cases of SJS/TEN occurring in consumers such as Plaintiff.⁴

D. Laws Governing the Approval and Labeling of Pharmaceutical Drugs

19. The facts of this case must be viewed against the backdrop of the regulatory framework and heightened duties of care imposed on drug makers. The Federal Food, Drug, and Cosmetic Act (“FDCA” or the “Act”) requires manufacturers that develop a new drug product to file a New Drug Application (“NDA”) in order to obtain approval from the Food and Drug Administration (“FDA”) before selling the drug in interstate commerce. 21 U.S.C. §355.

20. An NDA is the formal step a drug sponsor takes to request that the FDA consider approving a new drug for marketing in the United States. 21 C.F.R. §314.50. An NDA should include all animal and human data and analyses of the data, as well as information about how the drug behaves (pharmacokinetics and pharmacodynamics) in the body and how it is manufactured. 21 C.F.R. §314.50. A key component of the new drug approval process is the evaluation of the information regarding the safety and efficacy of the proposed drug. *Id.* Thus, the NDA must contain a section reporting on foreign or domestic clinical data regarding the proposed new drug. 21 C.F.R. §314.50(d)(5).

21. The application must also contain a description and analysis of all clinical studies (controlled or uncontrolled) relied upon in evaluating the safety and efficacy of the drug. 21 C.F.R. §314.50(d)(5)(ii). The NDA should also include “a description of any other data or information

⁴ FDA Guidance for Industry: Safety Reporting Requirements for INDs and BA/BE Studies (Dec. 2012), <https://www.fda.gov/downloads/Drugs/Guidances/UCM227351.pdf> (“Certain serious adverse events are informative as single cases because they are uncommon and are known to be strongly associated with drug exposure. Some examples, including...Stevens-Johnson syndrome.”).

relevant to an evaluation of the safety and effectiveness of the drug obtained or otherwise received by the applicant from any source, foreign or domestic, including commercial marketing experience, reports in the scientific literature, and unpublished scientific papers.” 21 C.F.R. §314.50(d)(5)(iv).

22. These FDA regulations in the premarketing phase require the drug sponsor to submit all safety information either to the IND or NDA – foreign or domestic – regardless of the source.⁵ Changes in foreign labeling should also be disclosed in the IND or NDA filings. *Id.*

23. Manufacturers with an approved NDA must review all adverse drug experience information obtained by or otherwise received by them from any source, including but not limited to post-marketing experience, reports in the scientific literature, and unpublished scientific papers. 21 C.F.R. §314.80(b).

24. Under what is known as the Changes Being Effected (“CBE”) regulation, a manufacturer with an approved NDA can make certain changes to its label without prior FDA approval by simply sending the FDA a “supplemental submission.” 21 C.F.R. §314.70(c)(6)(iii).

25. Changes to the labeling a manufacturer can make pursuant to CBE without prior FDA approval include those to “add or strengthen a contraindication, warning, precaution, or adverse reactions for which the evidence of causal association satisfies the standard for inclusion in the labeling under § 201.57(c) of this chapter” and “to add or strengthen an instruction about dosage and administration that is intended to increase the safe use of the drug product.” 21 C.F.R. §314.70(c)(6)(iii)(A) and (C).

26. A manufacturer must revise its label “to include a warning about a clinically significant hazard as soon as there is reasonable evidence of a causal association with a drug; a causal relationship need not have been definitively established.” 21 C.F.R. §201.57(c)(6). Adverse

⁵ Good Review Practice: Clinical Review of Investigational New Drug Applications, FDA, CDER, December 2013, p. 15, also citing FDA regulations, 21 C.F.R. §312.32; and FDA Reviewer Guidance, “Conducting a Clinical Safety Review of a New Product Application and Preparing a Report on the Review,” FDA CDER, February 2005.

reactions must be added to the label where there “is some basis to believe there is a causal relationship between the drug and the occurrence of the adverse event.” *Id.* at §201.57(c)(7).

27. An August 22, 2008 amendment to these regulations provides that a CBE supplement to amend the labeling for an approved product must reflect “newly acquired information.” 73 Fed. Reg. 49609. “Newly acquired information” is not limited to new data but also includes “new analysis of previously submitted data.” *Id.* “[I]f a sponsor submits adverse event information to FDA, and then later conducts a new analysis of data showing risks of a different type or of greater severity or frequency than did reports previously submitted to FDA, the sponsor meets the requirement for ‘newly acquired information.’” *Id.* at 49607.

28. The critical purpose of post marketing safety requirements is to ensure that the benefit of the drug outweighs the risk at all times during the life cycle of the product. 21 C.F.R. §§314.50, 314.80, and 314.81. If new safety information, including information from clinical trials, foreign countries or other information not previously disclosed to and considered by the FDA, comes to light that calls that balance into question, the FDA requires sponsors (like Defendants) to initiate risk management strategies to address the safety risk, including updating the drug label.

E. Defendants Have Known for Decades that Ibuprofen Causes SJS/TEN

29. The causal relationship between ibuprofen and serious skin reactions including SJS/TEN was first established over 40 years ago. Since then, leaders in the scientific community have repeatedly published articles identifying ibuprofen as a cause of SJS/TEN. Wyeth itself has conceded a “plausible causal relationship” between Advil and SJS/TEN, and Pfizer has conceded the same causal relationship in the physician’s prescription label for Motrin (ibuprofen):

NSAIDs, including MOTRIN tablets, can cause serious skin adverse events such as exfoliative dermatitis, Stevens-Johnson Syndrome (SJS), and toxic epidermal necrolysis (TEN), which can be fatal.

30. Consistent with the scientists, the regulators, and (sometimes) the Defendant drug companies, Plaintiff's treating burn surgeon at Wake Forest and the Director of the Wake Forest Burn Center have stated i) that ibuprofen is a known cause of SJS/TEN, and ii) Advil caused Plaintiff's SJS/TEN reaction. Despite their internal admissions and the overwhelming weight of the science, Defendants publicly deny and will deny in this case that ibuprofen can cause SJS and TEN. Defendants will also deny that Advil caused Plaintiff's SJS/TEN.

F. Newly Acquired Safety Information

31. Defendants have an independent legal duty to aggregate, analyze, and report on all adverse events and relevant scientific literature regarding the safety profile of Advil – including heightened risks to the female and South Asian (Indian) subpopulations occupied by Plaintiff – and to make necessary changes to their drug's label on an ongoing basis. Despite these health and safety obligations, Defendants continue to withhold and selectively report a host of significant new public information regarding the substantial risks of SJS/TEN caused by ibuprofen.

32. Following the FDA's approval of Advil, new safety information emerged that should have prompted Defendants to unilaterally change the Advil label without prior FDA approval (pursuant to the CBE-0 process in 21 C.F.R. §314.70) to warn for the increased risks of SJS/TEN. Defendants failed to disclose this important safety information to the FDA and have never attempted to add stronger warnings to the Advil label through the CBE-0 process or otherwise.

i. Undisclosed Cases of SJS and TEN (1985-2003)

33. Pfizer has marketed or licensed prescription ibuprofen products (under the Motrin brand, now licensed to and/or owned by Johnson & Johnson) since its predecessor, the Upjohn Company, received FDA approval for prescription Motrin in 1974. Accordingly, through its predecessors, Pfizer and the other Defendants are in possession of over 40 years of safety data related to serious skin reactions for ibuprofen products.

34. By at least 1982, two years before the FDA approved Advil for over-the-counter (“OTC”) OTC sale, Defendants knew there was a probable causal relationship between ibuprofen and SJS/TEN. Forty years have passed and – despite that known causal relationship – Defendants *to this day* have not conducted a comprehensive safety review for ibuprofen-related serious skin reactions. Nor have they reported all cases of SJS/TEN received either from spontaneous reporting or from their own clinical trials to the FDA, including two SJS/TEN cases that occurred in Advil pediatric clinical trials.

35. Pfizer’s subsidiary Wyeth placed Advil on the U.S. market in 1984. At the time, the Analgesic Therapeutic Team at Wyeth Consumer Healthcare was responsible for post-marketing surveillance (“PMS”) of Advil for safety signals or significant changes in its risk/benefit analysis. This responsibility included ongoing review of adverse event reports and scientific literature and reporting adverse event information associated with Advil products to the FDA. Even though Wyeth knew by 1995 that Advil-induced cases of SJS/TEN had occurred in pediatric clinical trials (including the Wyeth CAMP study), Wyeth misrepresented to the FDA that there were no cases of SJS/TEN in Advil trials. Wyeth’s Analgesic Therapeutic Team never conducted a risk assessment or safety signal analysis of SJS/TEN or disclosed to the FDA and U.S. consumers the significant safety information reported in the scientific literature regarding the risk of SJS/TEN from ibuprofen.

36. In 1997, Wyeth filed a Citizen's Petition⁶ requesting that the FDA switch Wyeth's Advil (200 mg ibuprofen) from operating under an NDA to a final monograph status that would categorize the 200 mg ibuprofen as a drug product that is generally recognized as safe and effective. Despite being required to do so, Wyeth again failed to report the safety data regarding SJS/TEN in its own Citizen's Petition or its supplemental submission to the FDA.

37. By 2000, when it transferred the pharmacovigilance and reporting requirements for Advil to Wyeth's Global Safety Surveillance and Epidemiology (GSSE), Wyeth was aware of at least 12 reports of SJS/TEN from Advil. The first PSUR⁷ generated by GSSE and submitted by Wyeth for single ingredient ibuprofen products was discussed at the Post-Market Safety Review meeting held by Wyeth on November 26, 2001. That meeting was attended by several representatives for Wyeth who were aware of the case reports of SJS/TEN. Wyeth's 2001 PSUR disclosed only one article about SJS/TEN associated with ibuprofen, even though several articles were published during this reporting period and should have been disclosed to the FDA and U.S. consumers. Wyeth at this time contended that the cases of SJS/TEN in its safety database did not provide evidence of a causal relationship between their product and SJS/TEN, even though its prescription product labeling for ibuprofen conceded a causal relationship.

38. In April 2002, Wyeth's next PSUR revealed that a case of SJS occurred during a clinical study and that Wyeth's study investigator identified a causal relationship between SJS and ibuprofen. The occurrence of even one report of SJS in a clinical study is a significant safety signal. However, Wyeth's Post-Marketing Safety Review team failed to investigate the signal and

⁶ A Citizen's Petition is a tool created by federal regulations to allow the public to request a specific action by a federal agency – here, the FDA.

⁷ A Periodic Safety Update Report (PSUR) is a pharmacovigilance document intended to provide an update of the safety experience of a drug to regulatory authorities at defined time points after approval of the drug.

risk and chose not to review and report the scientific literature containing cases of ibuprofen-induced SJS/TEN to the FDA.

39. Wyeth's October 2022 PSUR shows that there were 14 cases of SJS/TEN in the S3 (known as "S cubed") database associated with ibuprofen products. For the third time, Wyeth recommended that SJS/TEN be added to the Reference Safety Information (RSI) – the *internal labeling* used by the company to determine expectedness or compliance with regulatory post-marketing safety reporting. In contrast, Wyeth chose not to add an SJS/TEN warning to the over-the-counter external label for U.S. consumers.

40. Wyeth's April 2003 PSUR reported two additional cases of SJS/TEN associated with Children's Advil, and Wyeth admitted what it had known for decades: that a plausible causal relationship exists between SJS/TEN and Advil products.⁸

ii. The French Query (2003)

41. On April 30, 2003, the French government requested that Wyeth file an application to modify the labeling for Advil (known in France as the Summary of Product Characteristics or "SPC") to add a warning about SJS/TEN.

42. The French government asked Wyeth to provide an expert report and the spontaneous reports of SJS/TEN associated with Advil. GSSE, through Dr. Patricia Williams and Margaret Carr, conducted a search of SJS cases in Wyeth's database (only) and a cursory search of the literature.

43. The French government also conducted its own investigation and found that the ibuprofen literature reflected a clear safety signal for SJS. The French government also located several serious SJS and TEN cases that Wyeth did not disclose to it, concluded that TEN was more

⁸ This admission of a causal relationship was made by Wyeth officials as part of their overall conclusion about the safety of Advil products in another prior Advil SJS case styled *Lasandra Madden and Levell Madden, Individually and on Behalf of Labrea Williams, a minor child v. Wyeth, Inc., et al.*, No. 03-CV-0167 (N.D.Tex. 2003).

likely to be caused by ibuprofen than SJS, and recommended additional SJS/TEN warnings to the Advil label.

44. Wyeth objected to the warning language proposed by the French regulatory authorities and requested a three-month stay to prepare a defensive response, arguing to the French government that a warning about SJS/TEN was not required in the U.S. labeling and therefore should not be required in France.

45. In furtherance of its objection, Wyeth retained an expert, Dr. Daniel Julien, regarding the risks of SJS and TEN associated with ibuprofen. Dr. Julien concluded that SJS/TEN is caused by ibuprofen and further recommended that all NSAIDs and analgesics include an SJS/TEN warning. Despite their own expert's recommendations to add warnings about SJS/TEN to the Advil product labels, Wyeth continued to oppose the French government's recommendation for enhanced warning language, and further appealed the proposed labeling changes proposed by the French regulatory authorities.

46. Ultimately, the French government recommended that not only should SJS/TEN be listed in the SPC, but that both prescribers and consumers should be given warnings about the increased risks of SJS and TEN.

iii. The Citizen's Petition and Advil Label Change (2005)

47. In February 2005, Dr. Roger Salisbury and other concerned physicians and citizens, including parents of a three-year-old child who died from an SJS/TEN reaction from Advil, filed a Citizen's Petition requesting that the FDA perform a risk assessment and add new warnings regarding SJS/TEN for both prescription and OTC ibuprofen products.

48. The Citizen's Petition requested that action be taken by the FDA to require SJS-related warnings on all prescription and OTC ibuprofen products in order to protect Americans from the harm associated with SJS/TEN when using ibuprofen products, including Advil. The

Citizen's Petition did not include a request for a risk assessment specific to at-risk subpopulations (such as females and South Asians), nor was any such analysis conducted by the FDA or Defendants.

49. The following timeline summarizes significant events leading up to the 2005 Citizen's Petition:

- **1984:** FDA insists that a consumer leaflet accompany Advil box and bottle labeling as a condition of approval. By 1999, Defendants had unilaterally stopped distributing the leaflet with Advil products.
- **1993-1995:** Defendants learn of two documented cases of SJS occurring in Advil clinical pediatric trials and fail to properly report them to the FDA.
- **2001-2003:** Defendants submit PSURs reporting new reports of SJS/TEN in the pediatric population to French regulatory authorities, but do not submit them to the FDA. The French government requires SJS/TEN warnings for ibuprofen in France.
- **April 2003:** Defendants' PSUR for all Advil products admits that causality assessments of two reports of SJS/TEN in pediatric population establish a probable causal relationship for Advil (ibuprofen) and SJS/TEN. Defendants do not submit this PSUR to the FDA.
- **February 2005:** French regulatory authorities notify Defendants that stronger warnings regarding SJS/TEN will be added to the label of non-prescription Advil products in France.
- **May 2005:** In a May 25, 2005 letter, Defendants misrepresented to the FDA in writing that "the association of SJS/TEN with ibuprofen is tenuous at best."

50. Defendants filed a response to the Citizen's Petition with the FDA. Among other critical omissions, Defendants' FDA submission failed to disclose:

- two documented cases of SJS that occurred in Defendants' pediatric Advil trials;
- that the same Advil product label in France had been recently changed to add stronger warnings about the risks of SJS/TEN;
- that Defendants' retained expert, Dr. Julien, had concluded and advised Defendants that Advil causes SJS/TEN;

- that based on two spontaneous reports of SJS/TEN in the pediatric population, Defendants had internally determined that there was a probable causal relationship between Advil and SJS/TEN, as reported in a PSUR that was never filed or submitted to the FDA;
- that Defendants' retained expert report confirmed that ibuprofen had a "causal role" with regard to SJS/TEN;
- that, even though Defendants' ibuprofen products are marketed or licensed in over 60 countries, Defendants' submission to the FDA selectively sourced data from six countries and omitted critical regulatory actions (*e.g.*, French Query); and
- that Wyeth never conducted a risk assessment for subpopulations or tendered one to the FDA, even though Defendants had received a substantial number of SJS reports in the pediatric population including a report of death from TEN caused by Advil just one month prior to the submission.

51. Instead of disclosing this important safety information in May 2005, Defendants made the following misrepresentation in a written submission to the FDA:

Regarding Stevens-Johnson Syndrome (SJS) we have done an extensive review of the literature. Our review indicates that *there are a relatively small number of cases and the association of SJS/TEN with ibuprofen is tenuous at best.*

May 25, 2005 letter to FDA (emphasis supplied). Although 17 years have passed, Defendants have done nothing to correct their misleading statement to the FDA. In January 2006, still only a few months after denying to the FDA that Advil causes SJS/TEN, Defendants approved their prescription Motrin (ibuprofen) package insert stating that ibuprofen causes SJS/TEN.

52. The following timeline summarizes significant events leading up to the FDA's 2006 response to the Citizen's Petition:

- **February 16-18, 2005:** FDA holds joint advisory committee meetings with Defendants where no data is presented by Defendants regarding serious skin reactions from ibuprofen.
- **April 6, 2005:** FDA confirms its intent to add new warnings about skin reactions to OTC ibuprofen products. No specific warning language was proposed at that time.

- **April 7, 2005:** FDA signals that additional prescription and OTC labeling changes may occur upon completion of its review of the Citizen's Petition. FDA instructs Defendants to conduct a safety review of all Advil products (adult and pediatric) for cardiovascular and gastrointestinal safety information from their clinical trials and post-marketing data, but not for SJS/TEN.

53. On August 15, 2005, the FDA confirmed that the relief sought through the Citizen's Petition had been granted by requiring new warnings on both prescription and OTC labels for ibuprofen products. Despite being instructed to add these new warnings, Wyeth stubbornly maintained its position that there was not a proven causal relationship and continued to oppose the FDA's instruction to add the new warnings to the Advil label. The FDA denied Wyeth's request for reconsideration.

54. On October 3, 2005, Wyeth submitted proposed labeling changes to add the revised warning language. The new warning language was approved by the FDA in January 2006.

iv. Additional Scientific Literature Reporting an Increased Risk of SJS/TEN from Ibuprofen (2010-2022)

55. In 2012, Dr. William Soller, former Vice President of the Consumer Healthcare Products Association, the largest pharmaceutical trade group representing some of the largest drug companies in the world, conducted an independent study to compare revised and current ibuprofen OTC allergy alerts for usability, readability, and overall preferences in consumers naive to drug allergies and drug-induced allergy (DIA) survivors who experienced SJS/TEN from ibuprofen products.⁹

56. The article recommends that the OTC ibuprofen allergy warning should be revised to include language on time of onset, progression of severity, DIA risk, other symptoms, and to include the selective use of all capital letters. The author's proposed revised warning was strongly

⁹ Soller, W., "Improvement of the Drug Allergy Alert for Nonprescription NSAIDs," Drug Information Journal (May 2012) 46: 336-343, first published on April 10, 2012.

preferred by naive consumers¹⁰ and DIA survivors¹¹ over the current label. Similarly, the revised alert outperformed the current alert for ratings of usefulness for a person using ibuprofen for the first time. Over 92% of DIA survivors reported the revised alert covered most of their DIA signs/symptoms, and note that if they had the revised alert when experiencing their adverse drug reaction, they would have sought medical help sooner.

57. Defendants have not performed a similar labeling comprehension study to analyze whether the warnings for Advil adequately warn consumers regarding the risks of SJS/TEN. Defendants should have included this stronger warning language in the Advil label but chose not to do so.

58. In 2013, Pokhagul, P., et al.¹² published a study designed to identify and minimize the potential risks of serious and fatal adverse drug reactions, including serious skin reactions, in Thailand. Suspected adverse drug reactions (“ADRs”) reported to the Thai pharmaceutical agency between 1984 and 2011 were reviewed and analyzed by descriptive statistics. Ibuprofen was the leading cause of death among NSAIDs, due to SJS and TEN.

59. In January 2014, the Institute for Safe Medication Practices (ISMP) published their *QuarterWatch Special Report on Children*¹³ which is an independent publication that monitors all domestic, serious adverse drug events reported to the FDA. Ibuprofen was ranked in the top 10 in the author’s list of most frequent suspect drugs in serious adverse drug events, and produced unexpectedly large numbers of cases of SJS and TEN.

¹⁰ Naive consumers were those study participants who had not experienced a drug allergy and reviewed the current and proposed improved labeling.

¹¹ Survivors were consumers who had experienced a severe drug reaction and reviewed the current and proposed improved labeling.

¹² Pokhagul, et al. Utilization of ADR Reporting forward to Safety Laws and Regulations. Abstract Code: ISP3569-51, 13th ISO-P Annual Meeting: “The Renaissance of Pharmacovigilance” Pisa, Italy 01–04 October, 2013 *Drug Saf* (2013) 36:793–951.

¹³ Institute for Safe Medication Practices (ISMP) published their *QuarterWatch™ Special Report on Children*. January 16, 2014.

60. In 2014, Guy, et al.¹⁴ published a study of cases SJS and TEN reported to French regional pharmacovigilance centers (CRPV) between January 2002 and December 2011. Among the NSAIDs, ibuprofen had the highest number of SJS and TEN cases.

61. In 2015, Hung, et al.¹⁵ reported that between 1999-2011 ibuprofen was ranked in Taiwan as within the top 10 drugs for fatal reactions from SJS and TEN and had the third highest fatality rate of SJS and TEN among all other NSAIDs.

62. In 2015, Chodosh, et al.¹⁶ reported on their treatment of patients with ocular surface disease from SJS/TEN. Specifically, the authors reported on the visual outcomes of prosthetic replacement of the ocular surface ecosystem (PROSE) lens by using a retrospective cohort study at Harvard Medical School. They treated and analyzed 86 patients from January 1, 2006 to January 2011 with a history of SJS/TEN. The most common reported cause of SJS/TEN was ibuprofen (15 patients or 17% of all patients treated).

63. In 2016, Caverro-Carbonell, et al.¹⁷ performed an observational epidemiological analysis to study and describe the risk factors of SJS/TEN in a region in Spain's Rare Diseases Research Unit, SJS Registry, for the period of 2007-2013, using data validation which was performed by reviewing clinical documentation from hospital records. They reported that out of the 57 confirmed cases, the patients' SJS was mainly due to pharmacological treatments, and that ibuprofen caused more cases of SJS in the study population than any other drug.

¹⁴ Guy, C., et al., Drug-induced toxic epidermal necrolysis and Stevens-Johnson syndrome: analysis of the French national pharmacovigilance database. *9ème Congrès de Physiologie de Pharmacologie et de Thérapeutique Poitiers*, April 22-24, 2014, PM1-164.

¹⁵ Shuen-Iu Hung, PhD., Institute of Pharmacology, National Yang-Ming University, U.S. National Institute of Health (NIH): *SJS/TEN Workshop* (March 3-4, 2015).

¹⁶ Papakostas TD, Le H-G, Chodosh J, Jacobs DS. Prosthetic replacement of the ocular surface ecosystem as treatment for ocular surface disease in patients with a history of stevens-johnson syndrome/toxic epidermal necrolysis. *Ophthalmology* 2015;122(2):248-53.

¹⁷ Caverro-Carbonell, et al. Stevens Johnson Syndrome: identification of the risk factors in a rare disease. *European Journal of Public Health*, Sept. 2016, 26:376.

64. In 2016, Stocka-Labno E, et al.¹⁸ published their results from their epidemiological study of SJS and TEN to identify drugs and characterize population prone to these reactions. They retrospectively collected and reviewed medical records of 31 patients admitted to the Department of Dermatology from January 2009 to December 2014 at their hospital in Warsaw, Poland. They reported that ibuprofen was the most frequent cause of SJS/TEN, and that the number of cases attributed to ibuprofen were greater than every other category of medication.

65. In 2016, Miliszewski, M, et al.¹⁹ published the results from their study using a retrospective chart review that was conducted on 64 patients admitted to Vancouver General Hospital in Canada with a diagnosis of SJS or TEN between 2001 and 2011. The aim of their study was to identify the medications most often implicated in triggering SJS/TEN, as well as to delineate the timeline of identification and removal of the triggers. Ibuprofen was the leading cause of SJS and TEN among NSAIDs constituting 5% of the total patient population with SJS and TEN. It was also noted that Asians have an increased risk of death from SJS/TEN when compared to whites.

66. In 2017, Abdulah, R, et al.²⁰ published their study that aimed to identify the incidence, causative drugs, and economic consequences of these serious adverse drug reactions. The authors conducted a retrospective study that included 150 patients diagnosed with drug-induced SJS, or TEN from 2009 to 2013 in a hospital in Indonesia. The results showed that in Indonesia, analgesic-antipyretic drugs, including ibuprofen, were the most common cause of SJS and TEN in this population.

¹⁸ Stocka-Labno E, et al. Stevens-Johnson syndrome and toxic epidermal necrolysis in an academic hospital setting: a 5-year retrospective study. *Our Dermatol Online*. 2016;7(4):381-384.

¹⁹ Miliszewski, M, et al. Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis: An Analysis of Triggers and Implications for Improving Prevention. *The American Journal of Medicine* (2016) 129, 1221-1225.

²⁰ Abdulah, R, et al., Incidence, causative drugs, and economic consequences of drug-induced SJS, TEN, and SJS-TEN overlap and potential drug-drug interactions during treatment: a retrospective analysis at an Indonesian referral hospital. *Therapeutics and Clinical Risk Management* 2017;13 919-925.

67. In 2018, Rodríguez-Martín, et al.²¹ published their case-population study using a registry of SJS/TEN cases (PIELenRed) occurring between 2005-2015 and involving a study population from Madrid, Spain. The authors analyzed 44 cases of SJS/TEN and determined that the multivariate relative risk for new and current users of ibuprofen for SJS and TEN was 33. After controlling for confounding factors, the authors' analysis identified an association between ibuprofen and SJS/TEN.

68. In 2018, Micheletti, et al.²² published the first ever analysis by inpatient consultative dermatologists in the U.S. through their multicenter retrospective study, which included patients with SJS/TEN seen at 18 academic medical centers in the United States. A total of 377 adult patients with SJS/TEN between January 1, 2000 and June 1, 2015 were entered. Ibuprofen was one of the most frequent causes of SJS/TEN. Ibuprofen had more reports of confirmed SJS and TEN than all other NSAIDs, Tegretol and quinolone antibiotics.

69. In 2019, McPherson, et al. published updated guidelines for the management and treatment of SJS and TEN in young persons residing in the U.K. in 2018.²³ They noted that one of the most common drugs causing SJS/TEN in children and young people was ibuprofen. They also found that ibuprofen caused greater medical complications from SJS and TEN.

70. In 2022, Shao, Q, et al.²⁴ performed a data mining analysis of the FDA's Adverse Event Reporting System (FAERS) from January 2004 to March 2021. Among the five NSAIDs studied, ibuprofen had the highest association with SJS. Ibuprofen also had the highest SJS hospitalization rate among the NSAIDs.

²¹ Rodríguez-Martín, et al. Active surveillance of severe cutaneous adverse reactions: A case-population approach using a registry and a health care database. *Pharmacoepidemiol Drug Saf.* 2018;1-9.

²² Micheletti, R, et al. Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis: A Multicenter Retrospective Study of 377 Adult Patients from the United States. *J Invest Dermatol.* 2018 Nov;138(11):2315-2321.

²³ McPherson, et al. British Association of Dermatologists guidelines for the management of Stevens-Johnson syndrome/toxic epidermal necrolysis in children and young people 2018. *Br J Dermatol* 2019 Jul;181(1):37-54.

²⁴ Shao, S, et al. Stevens-Johnson Syndrome Following Non-steroidal Anti-inflammatory Drugs: A Real-World Analysis of Post-marketing Surveillance Data. *Front. Pediatr.* May 2022;10:1-7.

71. In violation of their legal duties described above, Defendants have not disclosed these articles and safety data to the FDA or warned U.S. consumers regarding the increased risks identified therein.

v. Female Subpopulation at Increased Risk of SJS/TEN

72. Since 1998, the FDA has required drug companies such as Defendants to follow the “Demographic Rule,”²⁵ which requires drug companies to assess and warn for subpopulation risks by age, gender, and racial subgroups.²⁶ Under the Demographic Rule, Defendants are required to assess subpopulation risk information from published and unpublished studies, the global scientific literature, data from the FDA’s adverse event database and their own Advil safety database, and provide subpopulation risk information in the warnings, precautions, and adverse reactions sections of the Advil labeling. 21 C.F.R. §314.50.

73. The FDA has stated that “research has shown that biological differences between men and women (differences due to sex chromosome or sex hormones) may contribute to variations seen in the safety and efficacy of drugs, biologics, and medical devices. The FDA’s regulations and guidance acknowledge that understanding mechanisms of sex differences in medical product development is crucial for regulatory decisions and optimal treatment outcomes.”²⁷

74. The available scientific literature shows that females are at a higher risk of SJS and TEN than males, yet Defendants’ Advil label draws no gender-based distinction. In 1986, Bigby and Arndt reported from the Boston Collaborative Drug Surveillance Program that, from June 1975 to June 1982, the incidence of cutaneous reactions was significantly higher (35%) in females

²⁵ 21 C.F.R §314.50(d)(5).

²⁶ FDA Guidance for Industry: Adverse Reactions Section of the Labeling for Human Prescription and Biological Products-Content and Format, March of 2006.

²⁷ <https://www.fda.gov/science-research/womens-health-research/understanding-sex-differences-fda>.

than in males.²⁸ Specifically, female patients have a 1.5 to 1.7-fold greater risk of developing an adverse drug reaction (“ADR”), including adverse skin reactions, compared with male patients.²⁹ A number of additional studies likewise suggest that ADRs are more frequent in women than in men.³⁰ In a UK study, the overall age-standardized odds ratio of ADR in females compared to males was 1.6 (95% CI 1.5 to 1.7).

75. In a large Italian study of ADRs in a population of 20 million people, cutaneous ADRs made up 45% of all reports with a female/male ratio of 1.58.³¹ Women presented more commonly with cutaneous reactions than males. Schopf, et al. also reported in 1990 from their epidemiological analyses of German cases of SJS and TEN that women were markedly more at risk for TEN by a ratio of 2:1. Roujeau reported in 2003 that the frequency/incidence between male:female ratio for TEN is 0.5:0.7. In 2007, Roujeau also reported that women had a higher risk of TEN. The table below sets out several additional articles that identify an increased risk of SJS and TEN in females:

Author	Years	Ratio	Percentage	Source of data
<i>Mockenhaupt, 2008 EuroSCAR</i>	1997-2001		62%	European, Israel
<i>Fen Gau, 2008</i>	1997-2004		51.4%	Taiwan
<i>Mockenhaupt, M, 2011</i>	Review		65%	Germany
<i>Bang, et al. 2012</i>	2007-2009		55.2%	India
<i>Weinand, et al. 2013</i>	1984-2011		3:2-SJS & 11:9-TEN	Germany
<i>Von Wild, et al. 2013</i>	2001-2011	2:1		Germany/ German Registry

²⁸ Bigby, M, “Drug-Induced Cutaneous Reactions: A report from the Boston Collaborative Drug Surveillance Program on 15,438 consecutive inpatients, from 1972-1982,” JAMA, 1986; 256:3358-3363.

²⁹ Rademaker, M., Am J Clin. Dermatol. “Do Women Have More Adverse Drug Reactions?” 2001; 2(6): pp.349-351.

³⁰ Pouyanne, P, et. al., “Admissions to Hospital caused by adverse drug reactions: cross sectional incidence study, BMJ, Vol. 320, pg. 1036, 2000; Fattinger, K, et. al., Br J Clin. Pharmacol., Epidemiology of drug exposure and adverse drug reactions in two Swiss departments of internal medicine, Vol. 49, pp. 158-67, 2000; Martin, RM, Br J Clin. Pharmacol., Age and Sex distribution of suspected adverse drug reactions to newly marketed drugs in general practice in England: analysis of 48 cohort studies, Vol. 46, pp. 505-511, 1998.

³¹ Naldi, L, et al., “Cutaneous reactions to drugs. An analysis of spontaneous reports in four Italian regions,” BCJP, 48, 839–846, 1999.

<i>Mockenhaupt, M, 2015</i>	Review		Greater than 50%	Most Countries Worldwide
<i>Hsu, et al. 2016</i>	2009-2012		58%	U.S.
<i>Diphhoorn, et al. 2016</i>	2009-2014	4:1		Italy
<i>Mockenhaupt, et al. 2018</i>	2003 to 2012	2:1		Germany/ German Registry
<i>Cairns, et al. 2020</i>	2009 - 2018		61%	U.S. UNC-Chapel Hill Burn Unit

Although Defendants have direct access to subpopulation risk data, they did not disclose the safety information above to the FDA and have never warned consumers of the increased risk of SJS and TEN in females.

vi. South Asian / Indian Subpopulation at Increased Risk of SJS/TEN

76. Certain ethnic subpopulations and genetic alleles can result in an increased risk of SJS and TEN. In 2012, Bang, et al.³² reported on their hospital-based study that analyzed patients who suffered SJS and TEN between June 2007 and September 2009 at Sheth Vadilal Hospital, Ahmedabad, India. The authors studied ibuprofen-related cases of SJS/TEN occurring in the Indian population and found that ibuprofen caused the highest number of cases of SJS and TEN (17.2%) among the study drugs and study population.

77. In 2016, Hsu, et al.³³ published the results of their general population study of the incidence, mortality, and costs of care for SJS and TEN in the U.S. adults. The Nationwide Inpatient Sample 2009-2012, containing a 20% sample of all US hospitalizations, was analyzed. The mean estimated incidences of SJS, and TEN were 9.2 and 1.9 per million adults per year, respectively. SJS/TEN was associated with higher risks in nonwhite races, particularly Asians (odds ratio= 3.27, 95% confidence interval = 3.02-3.54).

³² Bang, D., et al. Drug-induced Stevens–Johnson syndrome: case series from tertiary care center in Gujarat. *Pharmacoepidemiology and Drug Safety* 2012 Apr;21(4): 384-95.

³³ Hsu, et al. Morbidity and Mortality of Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis in United States Adults. *Journal of Investigative Dermatology* (2016) 136, 1387-1397.

78. Frey, et al.³⁴ conducted a large observational study on the epidemiology of SJS/TEN using data from the UK-based Clinical Practice Research Datalink. Among 551 validated SJS/TEN patients, they calculated an incidence rate of 5.76 SJS/TEN cases per million person-years between 1995 and 2013. Within a 1:4 matched case-control analysis, black and Asian patients were at a 2-fold risk of SJS/TEN when compared with white patients.

79. Although Defendants knew of the increased risks of SJS/TEN in the South Asian / Indian subpopulation, they did not disclosed this subpopulation risk data to the FDA or warn U.S. consumers of the increased risk of harm.

vii. Defendants Failed to Fully Report and Disclose Adverse Events and Safety Signal Analysis to the FDA

80. Under FDA regulations, Defendants are required to fully disclose all adverse event data received about the use of Advil in humans, both during the NDA process and afterward. Adverse drug events are important because drug companies use them to assess causality and to identify safety signals.

81. Ibuprofen has more reports of SJS and TEN than other drugs in its class. Defendants' own expert, Dr. Maja Mockenhaupt, published a paper in 2011 in which the authors reviewed spontaneous reports submitted to the FDA's AERS database and where the reports were restricted to suspect drugs for SJS, Lyell, EM and TEN.³⁵ Therein, the authors analyzed the AERS data from 1969 to the 4th quarter of 2009 and found that there were 295 reports of SJS and TEN for ibuprofen. Mockenhaupt, et al. also reported that the EB05³⁶ was elevated for ibuprofen. In

³⁴ Frey, et al. The Epidemiology of Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis in the UK. *Journal of Investigative Dermatology* (2017) 137, 1240-1247.

³⁵ Papay, et. al., "Spontaneous adverse event reports of Stevens-Johnson syndrome/toxic epidermal necrolysis: detecting associations with medications," *Pharmacoeconomics and Drug Safety*, Published online in Wiley Online Library (wileyonlinelibrary.com) DOI: 10.1002/pds.22.

³⁶ EB05 used in Papay, et al. is an adjusted estimate of the relative reporting rates from the U.S. FDA AERS database using the Multi-item Gamma Poisson Shrinker (MGPS), an empirical Bayes data-mining algorithm that runs on a web-based data-mining software application (Empirica Signal—Oracle Health Sciences).

fact, ibuprofen had more reports of SJS and TEN than any other NSAID in the FDA database and has the highest number of reports of SJS and TEN than the other OTC NSAIDs - by margins of 4 times higher than Aleve or naproxen.

82. As of the third quarter of 2009, the FDA AERS database³⁷ figures had grown to 295 validated reports of SJS/TEN from ibuprofen. In January 2010, the Lareb Pharmacovigilance Center report of World Health Organization (WHO) Vigibase data contained 397 reports of SJS/TEN from ibuprofen.

83. On information and belief, at the time of Plaintiff's injuries Pfizer possessed and was in part responsible for analyzing and reporting Advil-related adverse events to the FDA. On information and belief, even today, Defendants' adverse events are stored in Pfizer's safety database (Argus) and are directly accessible to Defendants at all times through Pfizer's electronic datamart, PfAST. Defendants failed to review and report to the FDA all serious cases of Advil-related adverse events, including cases of SJS, TEN, DRESS, AGEP, exfoliative dermatitis, bullous reactions, and related MedDRA terms.³⁸ Defendants further "soft coded"³⁹ relevant Advil adverse events and failed to adequately track, analyze and report safety signals that emerged from these reports of adverse events even though those safety signal reports and analysis are likewise directly available to Defendants through their safety signal database (Empirica) and safety signal tracking and monitoring system and log. In addition to the safety information discussed above, these adverse events, increase in adverse events reports and safety signal logs and analysis

³⁷ The FDA AERs database is a spontaneous adverse event reporting database.

³⁸ Section 505(k)(1) of the Federal Food, Drug, and Cosmetic Act and 21 C.F.R. §§314.80 and 314.81 require Defendants to establish and maintain records and to report data relating to clinical experience, along with other safety data or information for its drugs.

³⁹ "Soft coding" occurs when a drug company, during the adverse event data entry process, selects a medical term to code the adverse event that is less severe than the correct adverse event term.

constitute newly-acquired information that have not been fully reported to or analyzed by the FDA because Defendants did not disclose and properly report them to the FDA.

84. The substantial number of Advil-related adverse events in the FDA's FAERS database is concerning given the unprecedented marketing scheme Defendants implemented in an effort to sell Advil to as many U.S. and global consumers as possible. Since the 2006 Advil label change, there has been a total of 78,000 Advil and ibuprofen adverse events reported in FAERS.⁴⁰ A summary of relevant Advil and ibuprofen reporting numbers from 2006-2021 follows:

- Over 10,000 adverse events relate to skin reactions;
- 1,242 reports of SJS and TEN;
- 653 reports of TEN; and
- 145 deaths from SJS and TEN.

85. Plaintiff's allegation that Defendants failed to promptly investigate, review, and report all Advil-related serious adverse events is not without historical foundation. Pfizer has been cited by the FDA for failing to report serious adverse events. In 2010, the FDA issued a warning letter to Pfizer's Chief Executive Officer noting serious violations relating to Pfizer's adverse event reporting processes, including the following failures:

- "Failure to submit Adverse Drug Experience (ADE) reports to FDA as required by 21 C.F.R. 314.80(c)."
- "Serious and unexpected ADE reports are not promptly investigated as required by 21 C.F.R. 314.80(c)(1)(ii)."
- "Failure to submit 15-day Alert reports for serious adverse drug experiences as a non-applicant to the applicant within 5 calendar days of receipt as required by 21 C.F.R. 314.80(c)(1)(iii)."

⁴⁰ Defendants also routinely obtain spontaneous adverse event data from the World Health Organization, Uppsala Monitoring Center's safety database (Vigibase). Vigibase is the WHO global database of individual case safety reports (ICSRs). Defendants knew or should have known that the significant number of SJS/TEN and serious skin reaction reports in Vigibase also constituted another strong safety signal for Advil.

- “Failure to promptly review all adverse drug experience information obtained or otherwise received by the applicant from any source as required by 21 C.F.R. 314.80(b).”⁴¹

86. Defendants have continued to fail to adequately evaluate reports of ibuprofen-induced SJS, TEN, and serious skin reaction events, and failed to submit these serious adverse event reports to the FDA, including cases in the scientific literature and cases in Defendants’ own database. Plaintiff also alleges an increase in adverse events of SJS, TEN, and serious skin reactions events that have not been reported to, considered by or analyzed by the FDA due to Defendants’ wrongful conduct and withholding of safety information.

G. Conflict Between the Label and Medication Guide

87. The FDA-approved language for ibuprofen products that is shared with patients who get a *prescription* for ibuprofen products is different than the OTC language, but they are the same drug. The “Information for Patients” section for NSAIDs prescription labeling, including terms used in the Medication Guide, is written for consumers with an 8th grade education level of comprehension, and includes the following text:

Information for Patients

Patients should be informed of the following information before initiating therapy with an NSAID and periodically during the course of ongoing therapy. Patients should also be encouraged to read the NSAID Medication Guide that accompanies each prescription dispensed.

[Ibuprofen] tablets, like other NSAIDs, **can cause** serious skin side effects such as exfoliative dermatitis, SJS/TEN, **which may result in hospitalization and even death. Although serious skin reactions may occur without warning, patients should be alert for the signs and symptoms of skin rash and blisters, fever, or other signs hypersensitivity such as itching, and should ask for medical advice when observing any indicative sign or symptoms.** Patients should be advised to stop the drug immediately if they develop any type of rash and contact their physicians as soon as possible.

88. The FDA directed ibuprofen manufacturers, including Pfizer and Wyeth, to use this description of the risks of hospitalization or death and give that information to patients in

⁴¹ May 26, 2010 Warning Letter from FDA to Pfizer’s CEO Jeffrey Kindler.

prescription labeling. These warnings are not in the Advil OTC labeling. The prescription warnings also state that early symptoms can occur without warning, and caution patients to be alert for four different symptoms associated with a drug eruption or early bullous reaction.

89. The NSAID Medication Guide states, in an emphasized box, that serious side effects include:

- life-threatening skin reactions;
- life-threatening allergic reactions.

90. The NSAID Medication Guide further states:

“Stop your NSAID medicine and call your healthcare provider right away if you have any of the following symptoms: skin rash or blisters with fever.”

91. These descriptive terms are not (but should be) displayed on the OTC labeling for Advil products.

92. At the time of Plaintiff’s injuries in 2021, Defendants were the manufacturers, sellers and marketers for Advil in the majority of worldwide markets, including the U.S. Defendants controlled and/or had the right to control the safety initiatives of Advil labeling and warnings relating to Advil products; marketing initiatives and sales techniques; funding for sales, safety, development of the product; oversight of the safety data; and had control and/or the right to direct amendment and content of the labeling.⁴²

93. At the time of Plaintiff’s injury, Defendants’ Advil label misrepresented the safety of the product, stating in a severely understated manner, that “Ibuprofen may cause a severe allergic reaction, especially in people allergic to aspirin. Symptoms may include: hives, facial swelling, asthma (wheezing), shock, skin reddening, rash and blisters.” The deliberately understated listing of these “symptoms” is materially incomplete.

⁴² Plaintiff further alleges that Wyeth is the alter-ego of its parent company, Pfizer. Plaintiff contends that Pfizer is liable for all acts of negligence and other wrongful conduct of its wholly owned subsidiary, Wyeth, following its purchase of Wyeth pursuant to successor liability laws.

94. Plaintiff reviewed and relied on the entire Pfizer-labeled 200 mg Advil Liquid-Gel product label prior to using the product. Plaintiff's review of the Advil label included but was not limited to the uses and warnings sections. Among other stronger potential warnings, had Defendants warned Plaintiff of the serious risks of life-threatening skin reactions including SJS/TEN reactions; that death, disability, blindness, or hospitalizations can occur; warned of all of the early signs of a serious cutaneous adverse reaction (SCAR) event that Plaintiff herself experienced; or warned that South Asians / Indian and females (both of which were subclasses that Plaintiff occupied at the time of her ingestion of Advil) are at a higher risk of SJS/TEN and at an increased risk of a more severe injury from SJS/TEN (including an increased risk of severe ocular damage, as suffered by Plaintiff), then Plaintiff would not have taken Advil. An accurate, stronger, better and not misleading warning (including but not limited to the language contained above) would have prevented Plaintiff from taking Advil and suffering life-altering permanent injuries.

IV. CAUSES OF ACTION

A. NEGLIGENCE

95. Plaintiff incorporates by reference each and every paragraph of this Complaint as set forth in full herein.

96. Defendants had the duty to exercise ordinary and reasonable care in warning about, designing, testing, manufacturing, marketing, labeling, selling, and/or distributing Advil, including a duty to ensure that Advil did not cause users to suffer from unreasonable and dangerous side effects, including death, blindness, and other injuries.

97. Defendants failed to exercise ordinary and reasonable care in warning about, designing, testing, manufacturing, marketing, labeling, selling, and/or distributing Advil in that they:

- a. Failed to provide adequate warnings with Advil regarding its possible risks and adverse effects, as well as the comparative severity and duration of such adverse effects;
- b. Failed to conduct sufficient safety analysis on Advil, which if properly performed would have shown that Advil had serious side effects, including, but not limited to Stevens- Johnson Syndrome, TEN, and other serious side effects;
- c. Failed to adequately warn Plaintiff that use of Advil carried a risk of Stevens-Johnson Syndrome, TEN, and other life-threatening serious side effects;
- d. Failed to provide adequate post-marketing warning⁴³ or instructions after Defendants knew or should have known, of the significant risk of serious skin reactions to the use of Advil; and
- e. Placed an unsafe product into the stream of commerce.

98. As a direct and proximate result of the Defendants' negligence and sale of Advil without adequate warnings regarding the risk of serious skin reactions and other risks associated with its use as set forth above, Plaintiff suffered harm as alleged herein, including severe pain and suffering, loss of enjoyment of life, economic and non-economic loss, out-of-pocket costs of medical tests and treatment, future medical care and services, among other damages.

B. NEGLIGENCE MISREPRESENTATION

99. Plaintiff incorporates by reference each and every paragraph of this complaint as though set forth in full herein.

100. Defendants' label-based misrepresentations and omissions regarding the safety profile of Advil (as set forth above); failures to distribute consumer health updates and warnings outside of the product label; and misleading and incomplete advertising and promotion relating to the purported safe and effective qualities of the product, led to Plaintiff's purchase of Advil and caused Plaintiff to use Advil. Because the Advil label was misleading in the ways stated above

⁴³ Plaintiff's claims in this case are limited to post-NDA approval claims only.

and herein (including but not limited to an incomplete disclosure of the risk of injury and misleading nature of understatement of the side effects of Defendants' drug), Plaintiff relied on the language in the Advil label and ingested Advil, to Plaintiff's detriment and resulting in permanent disabling injury. But for these warning failures, misstatements and nondisclosures by Defendants, Plaintiff would not have taken Advil.

101. Defendants owed a duty to disseminate accurate and adequate information concerning Advil, and to exercise reasonable care to ensure that they did not, in those undertakings, create unreasonable risks of personal injury to others.

102. Defendants disseminated to consumers and Plaintiff, through product labeling, and other mediums, information concerning the efficacy, safety profile and understated side effects of Advil, with the intention that consumers and Plaintiff would rely upon that information when making a decision concerning whether to buy and use Advil.

103. Defendants breached their duty to ensure that the information contained in the label accompanying Advil is accurate, adequate, complete, and is not misleading. Defendants breached their duty to monitor the medical literature and post marketing adverse events and to report the data affecting the safety of the drug to the FDA.⁴⁴

104. Defendants knew that consumers like Plaintiff would rely upon Advil labeling and information disseminated from Defendants, and that many patients would be likely to ingest Advil as a result of Defendants' labeling and safety communications and advertising efforts.

105. Defendants made the misrepresentations in the Advil label and marketing materials referenced herein without any reasonable ground for believing them to be true. These misrepresentations were made directly by Defendants in the Advil labeling and in Defendant-

⁴⁴ Plaintiff is not bringing a claim for fraud on the FDA.

sponsored publications, Advil label and other written materials directed to Plaintiff with the intention of inducing reliance by Plaintiff.

106. The representations were in fact false and misleading and were intended to induce reliance on those misrepresentations and the purchase and use of Advil and Defendants knew or should have known that those misrepresentations would result in the ingestion of Advil by consumers such as Plaintiff. Plaintiff justifiably relied on Defendants' label-based representations to her detriment, which Defendants prepared and provided without reasonable care. Had Plaintiff known of the true facts and those facts concealed by Defendants, Plaintiff would not have purchased and ingested Advil and been injured. The reliance by Plaintiff at the time of purchase and October 2021 use of Advil on Defendants' misrepresentations was justified because such misrepresentations were made and conducted by Defendants, who were in a position to know and did know the true facts.

107. As a direct and proximate result of Defendants' negligent misrepresentations and breach of duty, Plaintiff suffered harm as alleged herein, including severe pain and suffering, loss of enjoyment of life, economic and noneconomic loss, out-of-pocket costs of medical tests and treatment, future medical care and services, among other damages.

C. GROSS NEGLIGENCE/WILLFUL AND WANTON CONDUCT

108. Plaintiff incorporates by reference each and every paragraph of this complaint as though set forth in full herein.

109. Defendants had the duty to exercise ordinary and reasonable care in manufacturing, marketing, labeling, selling, and/or distributing Advil including a duty to ensure that Advil did not cause users to suffer from unreasonable and dangerous side effects, like SJS and TEN.

110. Defendants failed to exercise ordinary and reasonable care in manufacturing, marketing, labeling, selling, and/or distributing Advil for the reasons set forth above.

111. As a direct and proximate result of the Defendants' sale of Advil without adequate warnings, Plaintiff suffered harm as alleged herein. Plaintiff's injuries have caused and continue to cause Plaintiff intense anxiety, distress, fear, loss of enjoyment of life, pain and suffering.

112. As a direct result of Defendants' gross negligence, willful and wanton misconduct, and other wrongdoing, which constitute conscious and reckless disregard for the rights and safety of others and a deliberate act or omission with knowledge of a high degree of probability of harm and reckless indifference to the consequences, Plaintiff was injured and suffered the damages for which she seeks recovery herein.

113. Defendants continued to promote the efficacy and safety of Advil, while providing little or no warnings, and downplayed the risks, even after Defendants knew of the risks and injuries associated with its use.

114. Defendants' conduct was committed with a willful, conscious or reckless disregard of and indifference to the rights and safety of consumers such as Plaintiff, thereby entitling Plaintiff to punitive damages in an amount to be determined at trial that is appropriate to punish Defendants and deter them from similar conduct in the future.

D. UNFAIR AND DECEPTIVE TRADE PRACTICE-MISREPRESENTATION

115. Plaintiff incorporates by reference each and every paragraph of this complaint as though set forth in full herein.

116. Defendants advertised, marketed and sold Advil. Defendants made representations of fact or promises to consumers, including Plaintiff, regarding the character or quality of Advil including, but not limited to, statements that Advil is safe and effective.

117. Advil was defective in that when it left the Defendants' possession in that it did not conform to Defendants' representations and did not conform to Plaintiff's expectations.

Defendants knew that the product did not conform to Defendants' representations when it was placed in the market.

118. Defendants knew that Advil was defective when it went to market. Defendants failed to give notice or warnings to consumers, including Plaintiff of the defective nature of the Advil. Defendants' conduct was immoral, unethical and substantially injurious to consumers such that constituted an unfair and deceptive trade practice.

119. Defendants' conduct was a direct and proximate cause of Plaintiff's injuries and damages. Defendants' conduct and practices occurred in commerce, were unfair and deceptive trade practices and entitle Plaintiff to treble her actual damages and recover attorney's fees, pursuant to the provisions of N.C.G.S. 75.1, *et seq.* and 75-16.1 *et seq.*⁴⁵

V. DEMAND FOR JURY TRIAL

120. Plaintiff demands a jury trial on all counts in this Complaint.

VI. REQUEST FOR RELIEF

Plaintiff respectfully requests judgment on each claim and relief as follows:

1. Actual and compensatory damages, including but not limited to past and future medical costs and services and past and future lost wages;
2. Past and future non-economic damages, including but not limited to past and future pain and suffering, disfigurement, loss of enjoyment of life, physical impairment, mental anguish, anxiety and discomfort;
3. Punitive and exemplary damages;
4. Damages and judgment for Unfair and Deceptive Trade Practices in an amount equal to treble the compensatory damages and Plaintiff's attorney fees pursuant to N.C. Gen. Stat. 75-16.1;
5. Pre-judgment and post-judgment interest; and
6. Plaintiff requests all other and further relief to which she is entitled at law and equity.

⁴⁵ *Dellinger v. Pfizer*, No. 5:03-cv-95, 2006 WL 2057654, at *4-5 (W.D.N.C. July 19, 2006) (denying Pfizer's motion for summary judgment on UDTPA claim where plaintiff alleged he was injured by Pfizer's drug Neurontin; holding, "there is no reason to exclude a consumer's personal injury from the category of injuries cognizable under the statute.").

DATED: April 28, 2023

/s/ Greg Jones

Greg Jones
North Carolina Bar No. 13001
greg@gregjoneslaw.com
GREG JONES LAW
1319 Military Cutoff Road
Suite CC, #138
Wilmington, NC 28405
Phone: 910.619.1100
greg@gregjoneslaw.com

Connor G. Sheehan*
Texas Bar No. 24046827
csheehan@dunnsheehan.com
DUNN SHEEHAN LLP
5910 N. Central Expressway, Suite 1310
Dallas, Texas 75206
Phone: 214.866.0077
Fax: 214.866.0070
**pro hac vice application forthcoming*

ATTORNEYS FOR PLAINTIFF